Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims

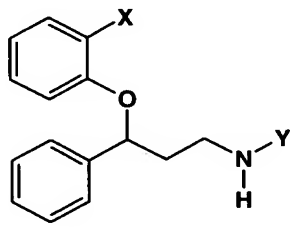
1. (currently amended): A method of preventing or treating hot flashes~~,~~ or vasomotor symptoms, ~~impulse control disorders, or personality change due to a general medical condition,~~ comprising administering to a patient in need thereof a therapeutically effective amount of a selective norepinephrine reuptake inhibitor selected from the group consisting of:

atomoxetine or a pharmaceutically acceptable salt thereof;

racemic reboxetine or a pharmaceutically acceptable salt thereof;

(S,S) reboxetine or a pharmaceutically acceptable salt thereof;

a compound of formula (I):

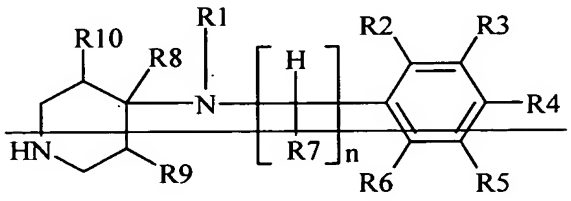


(I)

wherein X is C_1-C_4 alkylthio, and Y is C_1-C_2 alkyl, or a pharmaceutically acceptable salt thereof; and

a compound of formula (IH):

~~a compound of formula (IA):~~

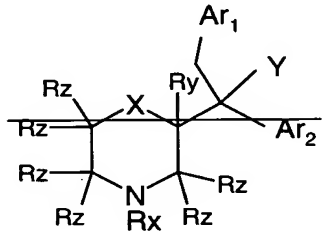


(IA)

~~wherein n is 1, 2 or 3; R1 is C_2-C_{10}alkyl, C_2-C_{10}alkenyl, C_3-C_8cycloalkyl or C_4-C_{10}cycloalkylalkyl, wherein one C-C bond within any cycloalkyl moiety is optionally substituted by an O-C, S-C or C=C bond and wherein each group is optionally substituted with from 1 to 7 halogen substituents and/or with from 1 to 3 substituents each independently selected from hydroxy, cyano, C_1-C_4alkyl, C_1-C_4alkylthio (optionally substituted with from 1 to 3 halogen atoms) and C_1-C_4alkoxy (optionally substituted with from 1 to 3 halogen atoms); R2 is H, C_1-C_4alkyl (optionally substituted with from 1 to 7 halogen atoms), C_1-C_4alkyl-$S(O)_x$- wherein x is 0, 1 or 2 (optionally substituted with from 1 to 7 halogen atoms), C_1-C_4alkoxy (optionally substituted with from 1 to 7 halogen atoms), cyano, halogen, phenyl (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C_1-C_4alkyl and C_1-C_4alkoxy), phenoxy (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C_1-C_4alkyl and C_1-C_4alkoxy) or -CO_2(C_1-C_4alkyl), or together with R3 forms a further benzene ring (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C_1-C_4alkyl and C_1-C_4alkoxy); R3 is H, C_1-C_4alkyl (optionally substituted with from 1 to 7 halogen atoms), C_1-C_4alkyl-$S(O)_x$- wherein x is 0, 1 or 2 (optionally substituted with from 1 to 7 halogen atoms), C_1-C_4alkoxy (optionally substituted with from 1 to 7 halogen atoms), cyano, halogen, phenyl (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C_1-C_4alkyl and C_1-C_4alkoxy), phenoxy (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C_1-C_4alkyl and C_1-C_4alkoxy) or -CO_2(C_1-C_4alkyl), or together with R2 or R4 forms a further benzene ring (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C_1-C_4alkyl and C_1-C_4alkoxy); R4 is H, C_1-C_4alkyl (optionally substituted with from 1 to 7 halogen atoms), C_1-C_4alkyl-$S(O)_x$- wherein x is 0, 1 or 2 (optionally substituted with from 1 to 7 halogen atoms), C_1-C_4alkoxy (optionally substituted with from 1 to 7 halogen atoms), cyano, halogen, phenyl (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C_1-C_4alkyl and C_1-C_4alkoxy), phenoxy (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C_1-C_4alkyl and C_1-C_4alkoxy) or -CO_2(C_1-C_4alkyl), or together with R3 forms a further benzene ring (optionally substituted with from 1 to 3 substituents each~~

~~independently selected from halogen, C_1-C_4alkyl and C_1-C_4alkoxy); R5 is H, C_1-C_4alkyl (optionally substituted with from 1 to 7 halogen atoms), C_1-C_4alkoxy (optionally substituted with from 1 to 7 halogen atoms) or halogen; R6 is H, C_1-C_4alkyl (optionally substituted with from 1 to 7 halogen atoms), C_1-C_4alkoxy (optionally substituted with from 1 to 7 halogen atoms) or halogen; R7 is H or C_1-C_4alkyl; R8 is H or C_1-C_4alkyl; R9 is H, halogen, hydroxy, cyano, C_1-C_4alkyl or C_1-C_4alkoxy; and R10 is H, halogen, hydroxy, cyano, C_1-C_4alkyl or C_1-C_4alkoxy; or a pharmaceutically acceptable salt thereof, with the proviso that the compound N-ethyl-N-benzyl-4-piperidinamine is excluded;~~

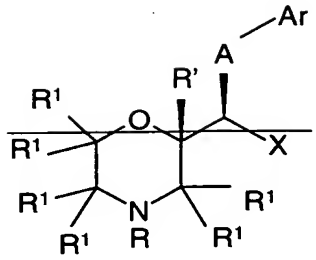
~~a compound of formula (IB):~~



~~(IB)~~

~~wherein Rx is H; Ry is H or C_1-C_4-alkyl; each Rz is independently H or C_1-C_4-alkyl; X represents O; Y represents OH or OR; R is C_1-C_4-alkyl; Ar_1 is a phenyl ring or a 5- or 6-membered heteroaryl ring each of which may be substituted with 1, 2, 3, 4 or 5 substituents (depending upon the number of available substitution positions) each independently selected from C_1-C_4-alkyl, O(C_1-C_4-alkyl), S(C_1-C_4-alkyl), halo, hydroxy, pyridyl, thiophenyl and phenyl optionally substituted with 1, 2, 3, 4 or 5 substituents each independently selected from halo, C_1-C_4-alkyl, or O(C_1-C_4-alkyl); and Ar_2 is a phenyl ring or a 5- or 6-membered heteroaryl ring each of which may be substituted with 1, 2, 3, 4 or 5 substituents (depending upon the number of available substitution positions) each independently selected from C_1-C_4-alkyl, O(C_1-C_4-alkyl) and halo; wherein each above-mentioned C_1-C_4-alkyl group is optionally substituted with one or more halo atoms; or a pharmaceutically acceptable salt thereof;~~

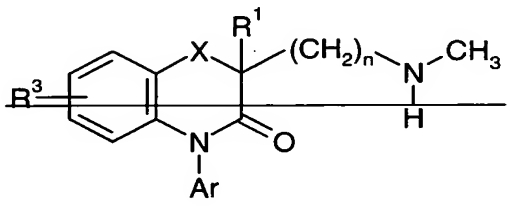
~~a compound of formula (IC)~~



~~(IC)~~

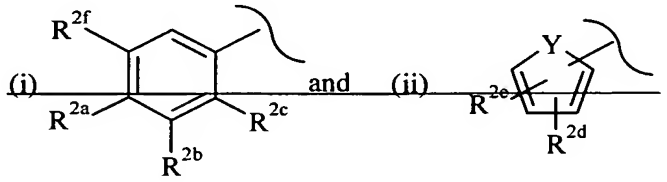
~~wherein: A is S or O; R is H; Ar is a phenyl group optionally substituted with 1, 2, 3, 4 or 5 substituents each independently selected from C_1-C_4 alkyl, O(C_1-C_4 alkyl), S(C_1-C_4 alkyl), halo, hydroxy, CO_2(C_1-C_4 alkyl), pyridyl, thiophenyl and phenyl optionally substituted with 1, 2, 3, 4 or 5 substituents each independently selected from halo, C_1-C_4 alkyl, or O(C_1-C_4 alkyl); X is a phenyl group optionally substituted with 1, 2, 3, 4 or 5 substituents each independently selected from halo, C_1-C_4 alkyl, or O(C_1-C_4 alkyl); a C_1-C_4 alkyl group; a C_3-C_6 cycloalkyl group or a CH_2(C_3-C_6 cycloalkyl) group; R' is H or C_1-C_4 alkyl; each R^1 is independently H or C_1-C_4 alkyl; wherein each above-mentioned C_1-C_4 alkyl group is optionally substituted with one or more halo atoms; or a pharmaceutically acceptable salt thereof; with the proviso that, when A is O, X is a C_1-C_4 alkyl group, a C_3-C_6 cycloalkyl group or a CH_2(C_3-C_6 cycloalkyl) group;~~

~~a compound of formula (ID)~~



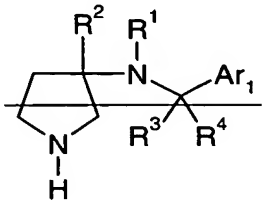
~~(ID)~~

~~wherein X is C(R^4R^5), O or S; n is 2 or 3; R^1 is H or C_1-C_4 alkyl; R^3 is H, halo, C_1-C_4 alkyl, O(C_1-C_4 alkyl), nitrile, phenyl or substituted phenyl; R^4 and R^5 are each independently selected from H or C_1-C_4 alkyl; Ar is selected from the group consisting of~~



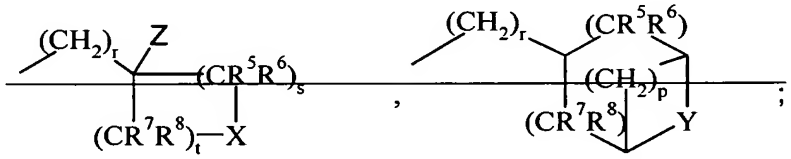
~~in which R^{2a} is H, halo, methyl or ethyl; R^{2b} is H, halo or methyl; R^{2c} is H, halo, methyl, trifluoromethyl, nitrile, or methoxy; R^{2d} is H, halo, methyl or ethyl; R^{2e} is H, halo, methyl, trifluoromethyl, nitrile, or methoxy; R^{2f} is H, or fluoro; Y is O, S or $N(R^6)$; and R^6 is H or methyl or a pharmaceutically acceptable salt thereof;~~

~~a compound of formula (IE)~~



~~(IE)~~

~~wherein R^1 is C_1-C_6 alkyl (optionally substituted with 1, 2 or 3 halo substituents and/or with 1 substituent selected from S (C_1-C_3 alkyl), O (C_1-C_3 alkyl) (optionally substituted with 1, 2 or 3 F atoms), O (C_3-C_6 cycloalkyl), SO_2 (C_1-C_3 alkyl), CN, COO (C_1-C_2 alkyl) and OH); C_2-C_6 alkenyl; $(CH_2)_q$-Ar_2; or a group of formula (i) or (ii)~~

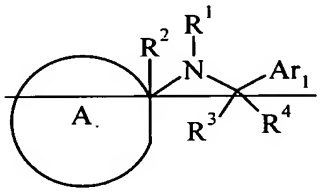


~~(i) (ii)~~

~~R^2, R^3 and R^4 are each independently selected from hydrogen or C_1-C_2 alkyl; R^5, R^6, R^7 and R^8 are at each occurrence independently selected from hydrogen or C_1-C_2 alkyl; X is a bond, CH_2, CH=CH, O, S, or SO_2; Y is a bond, CH_2 or O; Z is hydrogen, OH or O (C_1-C_3 alkyl); p is 0, 1 or 2; q is 0, 1 or 2; r is 0 or 1; s is 0, 1, 2 or 3; t is 0, 1, 2 or 3; Ar_1 is phenyl, pyridyl, thiazolyl, benzothiophenyl or naphthyl; wherein said phenyl, pyridyl or thiazolyl group may be substituted with 1, 2 or 3 substituents each independently selected from halo, cyano, C_1-C_4 alkyl (optionally substituted with 1, 2 or 3 F atoms), O (C_1-C_4 alkyl) (optionally substituted with 1, 2 or 3 F atoms) and S (C_1-C_4 alkyl) (optionally substituted with 1, 2 or 3 F atoms) and/or with 1 substituent selected from pyridyl, pyrazole, phenyl (optionally substituted with 1, 2 or 3 halo substituents) and phenoxy (optionally substituted with 1, 2 or 3 halo substituents); and wherein said benzothiophenyl or naphthyl group may be optionally substituted with 1, 2 or 3 substituents each independently selected from halo, cyano, C_1-C_4 alkyl (optionally substituted with 1, 2 or 3 F atoms), O (C_1-C_4 alkyl) (optionally substituted with 1, 2 or 3~~

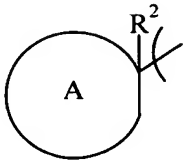
~~F atoms), and -S-(C_1-C_4 alkyl) (optionally substituted with 1, 2 or 3 F atoms); Ar_2 is naphthyl, pyridyl, thiazolyl, furyl, thiophenyl, benzothiophenyl, or phenyl, wherein said naphthyl, pyridyl, thiazolyl, furyl, thiophenyl, benzothiophenyl, or phenyl may be substituted with 1, 2 or 3 substituents each independently selected from halo, C_1-C_4-alkyl (optionally substituted with 1, 2 or 3 F atoms) and -O-(C_1-C_4-alkyl) (optionally substituted with 1, 2 or 3 F atoms); or a pharmaceutically acceptable salt thereof; provided that (a) the cyclic portion of the group of formula (i) must contain at least three carbon atoms and not more than seven ring atoms; (b) when -X- is -CH=CH-, then the cyclic portion of the group of formula (i) must contain at least five carbon atoms; and (c) when -Z is -OH or -O-(C_1-C_3-alkyl), then -X- is $-CH_2-$; (d) when -Y- is -O- then p cannot be 0; and (e) the compound 3-[(phenylmethyl)-(3S)-3-pyrrolidinylamino]-propanenitrile is excluded;~~

~~a compound of formula (IF)~~

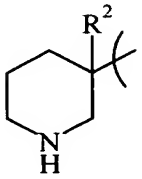


~~(IF)~~

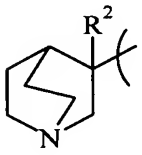
~~wherein~~



is a group of formula (a) or (b)



or

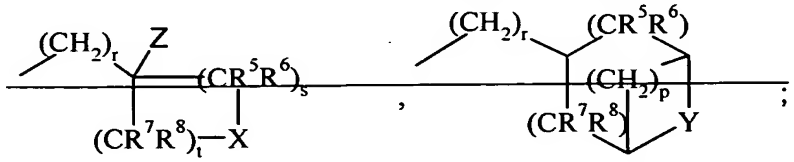


;

~~(a)~~ ~~(b)~~

~~R^1 is C_1-C_6 alkyl (optionally substituted with 1, 2 or 3 halo substituents and/or with 1 substituent selected from -S-(C_1-C_3-alkyl), -O-(C_1-C_3-alkyl) (optionally substituted with 1, 2-~~

~~or 3 F atoms), -O-(C_3-C_6 cycloalkyl), -SO_2-(C_1-C_3 alkyl), -CN, -COO-(C_1-C_2 alkyl) and -OH); C_2-C_6 alkenyl; -$(CH_2)_q$-Ar_2; or a group of formula (i) or (ii)~~



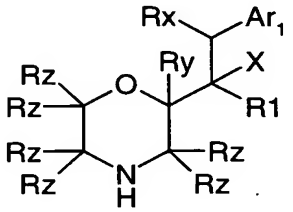
~~(i) (ii)~~

~~R^2, R^3 and R^4 are each independently selected from hydrogen or C_1-C_2 alkyl; R^5, R^6, R^7 and R^8 are at each occurrence independently selected from hydrogen or C_1-C_2 alkyl; X is a bond, CH_2, CH=CH, O, S, or SO_2; Y is a bond, CH_2 or O; Z is hydrogen, -OH or -O-(C_1-C_3 alkyl); p is 0, 1 or 2; q is 0, 1 or 2; r is 0 or 1; s is 0, 1, 2 or 3; t is 0, 1, 2 or 3; Ar_1 is phenyl, pyridyl, thiazolyl, benzothiophenyl or naphthyl; wherein said phenyl, pyridyl or thiazolyl group may be substituted with 1, 2 or 3 substituents each independently selected from halo, cyano, C_1-C_4 alkyl (optionally substituted with 1, 2 or 3 F atoms), -O-(C_1-C_4 alkyl) (optionally substituted with 1, 2 or 3 F atoms) and -S-(C_1-C_4 alkyl) (optionally substituted with 1, 2 or 3 F atoms) and/or with 1 substituent selected from pyridyl, pyrazole, phenyl (optionally substituted with 1, 2 or 3 halo substituents), benzyl and phenoxy (optionally substituted with 1, 2 or 3 halo substituents); and wherein said benzothiophenyl or naphthyl group may be optionally substituted with 1, 2 or 3 substituents each independently selected from halo, cyano, C_1-C_4 alkyl (optionally substituted with 1, 2 or 3 F atoms), -O-(C_1-C_4 alkyl) (optionally substituted with 1, 2 or 3 F atoms), and -S-(C_1-C_4 alkyl) (optionally substituted with 1, 2 or 3 F atoms); Ar_2 is naphthyl, pyridyl, thiazolyl, furyl, thiophenyl, benzothiophenyl, or phenyl, wherein said naphthyl, pyridyl, thiazolyl, furyl, thiophenyl, benzothiophenyl, or phenyl may be substituted with 1, 2 or 3 substituents each independently selected from halo, C_1-C_4 alkyl (optionally substituted with 1, 2 or 3 F atoms) and -O-(C_1-C_4 alkyl) (optionally substituted with 1, 2 or 3 F atoms); or a pharmaceutically acceptable salt thereof; provided that (a) the cyclic portion of the group of formula (i) must contain at least three carbon atoms and not more than seven ring atoms; (b) when X is CH=CH, then the cyclic portion of the group of formula (i) must contain at least five carbon atoms; and (c) when Z is -OH or -O-(C_1-C_3 alkyl), then X is CH_2; and (d) when Y is O then p cannot be 0;~~

~~a compound of formula (IG)~~

~~(IG)~~

~~R^2 is C_1-C_4 alkyl, phenyl or phenyl substituted with 1, 2 or 3 substituents each independently selected from C_1-C_4 alkyl, C_1-C_4 alkoxy, nitro, hydroxy, cyano, halo, trifluoromethyl, trifluoromethoxy, benzyl, benzyloxy, NR^6R^7, $CONR^6R^7$, $COOR^6$, $SO_2NR^6R^7$ and SO_2R^6; R^5 is selected from C_1-C_4 alkyl, C_1-C_4 alkoxy, carboxy, nitro, hydroxy, cyano, halo, trifluoromethyl, trifluoromethoxy, benzyl, benzyloxy, NR^8R^9, $CONR^8R^9$, $SO_2NR^8R^9$ and SO_2R^8; R^3, R^4, R^6, R^7, R^8 and R^9 are each independently selected from H or C_1-C_4 alkyl; and Z is a bond, CH_2, or O; or a pharmaceutically acceptable salt thereof and~~



(IH)

wherein,

X is OH, C1-C4 alkoxy, NH_2, or NH(C1-C4 alkyl);

Rx is H or C1-C4 alkyl;

Ry is H or C1-C4 alkyl;

each Rz group is independently H or C1-C4 alkyl, with the proviso that not more than 3 Rz groups may be C1-C4 alkyl;

R1 is C1-C6 alkyl ~~(~~optionally substituted with 1, 2 or 3 halogen atoms and/or with 1 substituent selected from the group consisting of C1-C4 alkylthio ~~(~~optionally substituted with 1, 2 or 3 fluorine atoms~~)~~, C1-C4 alkoxy ~~(~~optionally substituted with 1, 2 or 3 fluorine atoms~~)~~, C3-C6 cycloalkoxy, C1-C4 alkylsulfonyl, cyano, -CO-O(C1-C2 alkyl), -O-CO-(C1-C2 alkyl), and hydroxy~~)~~; C2-C6 alkenyl ~~(~~optionally substituted with 1, 2 or 3 halogen atoms~~)~~; C3-C6 cycloalkyl ~~(~~optionally substituted with 1, 2 or 3 halogen atoms and/or with 1 substituent selected from the group consisting of C1-C4 alkoxy and hydroxyl~~)~~ wherein one C-C bond within the cycloalkyl moiety is optionally substituted by an O-C, S-C or C=C bond; C4-C7 cycloalkylalkyl ~~(~~optionally substituted with 1, 2 or 3 halogen atoms and/or with 1 substituent selected from the group consisting of C1-C4 alkoxy and hydroxyl~~)~~ wherein one C-C bond within the cycloalkyl moiety is optionally substituted by an O-C, S-C or C=C bond; or CH_2Ar2; and

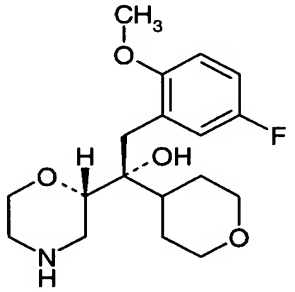
Ar1 and Ar2 are each independently a phenyl ring or a 5- or 6-membered heteroaryl ring each of which is optionally substituted with 1, 2 or 3 substituents (depending upon the number of available substitution positions,) each independently selected from the group consisting of C1-C4 alkyl (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkoxy (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkylthio (optionally substituted with 1, 2 or 3 halogen atoms), -CO-O(C1-C4 alkyl), cyano, -NRR, -CONRR, halo, and hydroxyl, and/or with 1 substituent selected from the group consisting of pyridyl, thiophenyl, phenyl, benzyl, and phenoxy, each of which is optionally ring-substituted with 1, 2 or 3 substituents each independently selected from the group consisting of halogen, C1-C4 alkyl (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkoxy (optionally substituted with 1, 2 or 3 halogen atoms), carboxy, nitro, hydroxy, cyano, -NRR, -CONRR, SO_2NRR, and SO_2R); and each R is independently H or C1-C4 alkyl;

or a pharmaceutically acceptable salt thereof.

2. (cancelled)

3. (currently amended): The method of claim 1 ~~or the use of claim 2~~, wherein said selective norepinephrine reuptake inhibitor is atomoxetine hydrochloride.

4. (new): The method of claim 1, wherein said selective norepinephrine reuptake inhibitor is a compound of the formula:



or a pharmaceutically acceptable salt thereof.

5. (new): The method of claim 4, wherein said compound is in the form of a hydrochloride salt.